According to the Paperwork Reduction Act of 1995, an agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0579-0036. The time required to complete this information collection is estimated to average 2 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

OMB APPROVED
0579-0036
Exp.: 10/31/2018

This report is required by law (7 U.S.C. 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

Interagency Report Control
No. 0180-DOA-AN

Fiscal Year 2013

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. REGISTRATION NUMBER
94-R-0109

2. HEADQUARTERS RESEARCH FACILITY *(Name, address, and telephone number as registered with USDA, include ZIP Code)*

UNIVERSITY OF PUERTO RICO
PO BOX 365067 - MEDICAL SCIENCE CAMPUS

SAN JUAN, PR 00936

3. REPORTING FACILITY *(List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets, if necessary.)*

FACILITY LOCATIONS *(Sites)*

(b)(7)(F)

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets, if necessary, or use APHIS FORM 7023A.)*

A. Animals Covered By The Animal Welfare Regulations	**B.** Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	**C.** Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	**D.** Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	**E.** Number of animals upon which teaching, experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress on these animals and the reasons such drugs were not used must be attached to this report.)*	**F.** TOTAL NUMBER OF ANIMALS **(Cols. C + D + E)**
4. Dogs	0	0	0	0	0
5. Cats	0	0	0	0	0
6. Guinea Pigs	0	0	0	0	0
7. Hamsters	0	0	0	0	0
8. Rabbits	0	0	10	0	10
9. Non-human Primates	0	4076	324	22	4422
10. Sheep	0	0	0	0	0
11. Pigs	0	0	27	0	27
12. Other Farm Animals					
13. Other Animals					

ASSURANCE STATEMENTS

1.) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2.) Each principal investigator has considered alternatives to painful procedures.

3.) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4.) The attending veterinarian for this research facility has appropriate authority to ensure the provisions of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL

(*Chief Executive Officer (C.E.O.) or Legally Responsible Institutional Official (I.O.)*)

I certify that the above is true, correct, and complete (7 U.S.C. Section 2143).

SIGNATURE OF C.E.O. OR I.O.	**NAME AND TITLE OF C.E.O. OR I.O.** *(Type or Print)*	**DATE SIGNED**
(b)(6), (b)(7)(c)		28-JAN-2014

According to the Paperwork Reduction Act of 1995, an agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0579-0036. The time required to complete this information collection is estimated to average 2 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

OMB APPROVED
0579-0036
Exp.: 10/31/2018

This report is required by law (7 U.S.C. 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

Interagency Report Control No. 0180-DOA-AN

Fiscal Year 2013

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. REGISTRATION NUMBER
94-R-0114

2. HEADQUARTERS RESEARCH FACILITY *(Name, address, and telephone number as registered with USDA, include ZIP Code)*

UNIVERSIDAD INTERAMERICANA DE PUERTO RICO
500 CARR JOHN WILL HARRIS

BAYAMON, PR 00957

3. REPORTING FACILITY *(List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets, if necessary.)*

FACILITY LOCATIONS *(Sites)*

(b)(7)(F)

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets, if necessary, or use APHIS FORM 7023A.)*

A. Animals Covered By The Animal Welfare Regulations	**B.** Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	**C.** Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	**D.** Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	**E.** Number of animals upon which teaching, experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress on these animals and the reasons such drugs were not used must be attached to this report.)*	**F.** TOTAL NUMBER OF ANIMALS **(Cols. C + D + E)**
4. Dogs	0	0	0	0	0
5. Cats	0	0	0	0	0
6. Guinea Pigs	0	0	0	0	0
7. Hamsters	0	0	0	0	0
8. Rabbits	0	0	0	0	0
9. Non-human Primates	0	0	0	0	0
10. Sheep	0	0	0	0	0
11. Pigs	0	0	0	0	0
12. Other Farm Animals					
13. Other Animals					

ASSURANCE STATEMENTS

1.) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2.) Each principal investigator has considered alternatives to painful procedures.

3.) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4.) The attending veterinarian for this research facility has appropriate authority to ensure the provisions of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL

(*Chief Executive Officer (C.E.O.) or Legally Responsible Institutional Official (I.O.)*)

I certify that the above is true, correct, and complete (7 U.S.C. Section 2143).

SIGNATURE OF C.E.O. OR I.O.	NAME AND TITLE OF C.E.O. OR I.O. *(Type or Print)*	DATE SIGNED
(b)(6), (b)(7)(c)		16-DEC-2013

OCT 22 2013

Attachment 1

Explanation for USDA Classification E

(This report is required to accompany USDA Form 7023 to support any USDA Classification E listings.)
This document must be typed.

CERTIFICATE #94-R-0109
CUSTOMER #960

Name of Investigator: (b) (6), (b) (7)(C)

Animal Study Proposal Title: **Familial circadian disorder in non-human primates**

Species and number of animals listed in Classification E for each year:

Species: Macaca mulatta COMMON NAME: RHESUS MONKEY

Number of Animals INCLUDED UNDER THESE EXCEPTIONS FOR FISCAL YEAR 2013 : 22

Description of project including reason (s) for species selection:

The Project will investigate the intrinsic and entrained circadian rhythms of sleep, activity, food intake and cognitive performance. Rhesus monkeys and humans have principal similarities in sleep process, circadian clock system and its temporal relationship with periodically changing body functions. As such, rhesus monkeys provide outstanding translational model for understanding human circadian system, its role in normal functioning of the organism and in pathological conditions.

Moreover, we have recently discovered the first circadian disorder in rhesus monkeys, with major similarities to human pathological circadian condition, the delayed sleep phase disorder (DSPD) and nighttime eating syndrome (NES). These human disorders do not have ready prophylactic or treatment strategies available. Thus, studies in a diurnal non-human primate model would allow for not only a search for the genetic bases of DSPD but also for testing prospective treatment strategies, as will be addressed in this Protocol.

Provide a scientific justification to explain why the use of anesthetics, analgesics, sedatives or tranquilizers during and/or following painful or distressing procedures is contraindicated:

Animals on this Protocol will NOT experience pain or distress. The only procedure that could induce pain will be an insertion of a catheter for blood withdrawal, and this will be conducted under general anesthesia.

The reasons for considering category "E" for these studies is in the two "unusual conditions" that are inherent to methodological approaches used to investigate intrinsic circadian rhythms in humans or other species: social isolation and

OCT 22 2013

periods of constant dim light illuminations. Together, those are required to ensure lack of environmental time cues (light-dark cycle) and entrainment to a social counterpart, thus allowing for revealing individual's intrinsic rhythms of behavioral and physiological functions, and the degree of their synchrony.

Overall Rational for Social Isolation: Individual animals and humans have different period of intrinsic rhythm and entrain to a light-dark cycle with a different phase angle between the light period and a certain rhythm phase, or have different temporal relationship between specific body rhythms (e.g., sleep and food intake, or hormonal secretion). Co-habitation significantly affects these phase relationships during entrainment and modifies an intrinsic period. Thus, studying individual's circadian rhythms and their adjustment to changes in environmental illumination requires social isolation. This approach is used in human studies of circadian rhythms as well.

Overall Rational for Constant dim light (CDL): Revealing individual's intrinsic circadian rhythm requires constant conditions, devoid of time cues. Hence, no light-dark cycle can be implemented during such studies. While regular light exposure (LD cycle) entrains humans and other animals, random light exposure disrupts or shifts the circadian clock, advancing or delaying it depending on the time of administration (so called, "phase response"). The CDL conditions are known not to induce stress, unlike constant darkness or constant bright light. Constant bright light also leads to sleep deprivation, lengthens the intrinsic period and inhibits circadian amplitude. For this reason, CDL is used in circadian studies conducted in both humans and diurnal non-human primates.

Without these two "unusual conditions", the intrinsic circadian rhythms cannot be assessed in humans or non-human primates.

Neither "unusual condition" was found to alter behavior, cognitive performance or food intake in adult non-human primates studied for over a year of social isolation, with intermittent exposure to CDL for several weeks at a time, as in this Protocol (Masuda et al 2010; Zhdanova et al, 2011; Zhdanova, et al, 2012). No other studies on circadian rhythms involving similar techniques reported distress in experimental animals, with the behavioral distress being judged based on self-injurious behavior, pacing, vocalization, hair plucking, etc. This is, in part, due to the special attention we pay to enrichment techniques in our studies, to alleviate any risk of unwanted effects of constant conditions.

The **principal enrichment technique** used in this Protocol is the goal-oriented interactive behavior, represented by an operation of interactive food-rewarding computerized device, equipped with a touch screen monitor, and self-determined feeding protocol. As in humans, motivation for goal-oriented behavior and its rewarding properties is a major cognitive enrichment. Moreover, we will provide a choice of video games and short video clips that animal can choose to initiate using the same touch screen monitor positioned in each chamber. Based on our long-term observations while conducting circadian studies in rhesus monkeys at Boston University, these techniques provide sufficient enrichment and prevent occurrence of behavioral abnormalities.

OCT 22 2013

Animals also receive different Kong toys. Every 10-14 days toys are replaced with new ones; the favorite toys are either provided more frequently or on the permanent basis (being washed/exchanged during chamber wash procedure).

In case an animal is unusually sensitive to social isolation or constant dim light conditions, and found to display novel abnormal behaviors, or increase in pre-existing condition (e.g., increase in pre-existing fur plucking or pacing), it will be provided with additional enrichment (e.g., toys, video games) and temporal re-introduction of social contact. If the condition is not attenuated within the next 10 days, or further augmented during this period, the animal will be removed from the circadian chamber and either placed into the social coral or individual cage for further observations.

Historically, we applied the category "E" to our Protocol, when run at BU, based on the "unusual conditions" of housing and lack of published data on the effects of these conditions on mature rhesus monkeys. Now, with scientifically established lack of negative effects of these conditions in mature rhesus monkeys, we could consider category "D" instead. We, however, would prefer the IACUC to define the category assignment, based on the information provided here, and will be glad to provide more details, if needed.

Provide a scientific justification to explain why the use of anesthetics, analgesics, sedatives or tranquilizers during and/or following painful or distressing procedures is contraindicated:

There will be NO experimentally-induced conditions on this Protocol that would require treatment.

(b) (6), (b) (7)(C)

Signature of Principal Investigator: [redacted] **Date:** 8/12/12

Signature of IACUC Chairperson: ____ **Date:** 10/22/12